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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,476	02/21/2001	Ching Ming Chung	3669-0103P	6205

2292 7590 10/24/2005

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FALLS CHURCH, VA 22040-0747

EXAMINER
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YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 10/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/788,476

Applicant(s)

CHUNG ET AL.

Examiner

MISOOK YU, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 15-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 15-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Exhibit A, and B.

### **DETAILED ACTION**

Prosecution on the merits of this application is reopened on all pending claims 1, and 15-17 which are considered unpatentable for the reasons indicated below. This Office action contains new grounds of rejection. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Objections***

Claim 1 is objected to because of the following informalities: the hybridizing species should be hybridized to the complement of the coding sequence, not the coding sequence itself in order to have the recited function. Inserting "the complement" after "hybridizes" in line 4 of claim 1 would obviate this rejection. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112***

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to an isolated nucleic acid comprising a nucleotide sequence having at least about 60% similarity to the full length of SEQ ID NO: 1, or 3 and that hybridizes to the complement of SEQ ID NO: 1 or 3 under the conditions of 0.1 x SSC buffer, 0.1 % w/v SDS at 65 degree Celsius, wherein an mRNA corresponding to said

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nucleic acid is differentially expressed in human hepatocellular carcinoma (HCC), or in human pancreatic adenocarcinoma.

The application discloses a single cDNA (SEQ ID NO: 1, note SEQ ID NO: 3 is the fragment of SEQ ID NO: 1), which encodes a human protein. The specification on page 37 discloses differential expressions of the corresponding mRNA in human hepatocellular carcinoma (HCC), and also in human pancreatic adenocarcinoma. The differential expression is detected using the first strand cDNA (i.e. SEQ ID NO: 1). There is a single species explicitly disclosed (SEQ ID NO: 1) that is within the scope of the claimed genus. Thus, there is actual reduction to practice of the disclosed species. The specification does not include any other species that meets the recited structural limitation, at least 60 % and hybridizes to the complement to SEQ ID NO: 1 or 3.

The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus.

The full scope of the claim encompasses naturally occurring allelic variants resulting from a different codon usage of a gene, isoforms resulting from an alternative splicing of a gene, or paralog resulting from gene duplication in a human genome, and others such as ESTs. This point will be elaborated with some example below. There are substantial variability among the species of nucleic acids encompassed within the

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scope of the claim, because of the limitation "at least about only 60 % similarity" in the claim. The hybridization conditions recited in the claim along with the recited function associated with the claimed genus does not narrow variability among the species of nucleic acids encompassed with the claimed scope.

The instantly recited high stringency and the hybridizing condition in hypothetical claim 1 of Example 9 in the USPTO Written Description Guidelines (the Guidelines) are almost identical.

Instant claim 1 reads:

An isolated nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3 or a nucleotide sequence, having at least about 60 % similarity to the full length of SEQ ID NO:1 or SEQ ID NO:3, that hybridizes to SEQ ID NO:1 or SEQ ID NO:3 under conditions of 0.1 x SSC buffer, 0.1% w/v SDS, at a temperature of at least 65 °C, wherein an mRNA corresponding to said nucleic acid is differentially or preferentially expressed in human hepatocellular carcinoma tissue or tissue from pancreatic adenocarcinoma relative to other tissue in said subject and/or in subject not diagnosed with this condition.

The hypothetical Claim 1 of Example 9 in the Guidelines reads:

An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

However, in the case of claim 1 of Example 9 in the Guidelines, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claim because the highly stringent hybridization condition set forth in the claim in combination with the coding function of the genus of nucleic acids, and the level of skill in and knowledge in the DNA recombinant and enzymatic activity detection art are adequate to determine that applicant was in possession of the claimed invention. In

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other words, the recited function in claim 1 of Example 9 is dictated by the chemical structure of the claimed genus. The highly stringent hybridization conditions along with the recited functional characteristic eliminates a vast number of species such as ESTs, especially EST comprising only the 3' untranslated region, which does not encode a protein with the recited function. However, unlike the situation in Example 9 of the Guidelines, the instantly recited function is not associated with the structural feature of claimed genera, but associated with human disease status. The claim language does not eliminate vast number of EST sequences. The claimed species hybridizing to the complement of SEQ ID NO: 1 or 3 under the high stringent conditions recited are not necessarily at least about 60 % similar to the full length of SEQ ID NO: 1 or 3 or vice versa. For example, one of sequence in the sequence alignment provided in the Office action mailed on 7/2/2002 is a 266 base pair EST, which matches 98.5 % from the nucleotide #21 to 285 of instant SEQ ID NO: 1. This EST sequence disclosed in WO9845435-A2 would hybridize to the instant SEQ ID NO: 1 under the recited high stringent conditions. However, the EST sequence is only 28.9 % to the full-length of instant SEQ ID NO:1. EST by definition is a sequence being expressed, thus most likely meet the function characteristic recited in the claim. However, the high stringency along with the instantly recited function does not exclude the short EST. Rather the limitation "60 %" to the full length of SEQ ID NO: 1 or 3 exclude this species. In short, the high stringent hybridization conditions along with the recited function do not yield similar DNAs, but leads to substantial variation among the species.

In addition, the expression is not function associated with the structure but a reaction of a human body to certain stimuli, in the instant case the development of HCC or pancreatic adenocarcinoma. The recited function is not dictated by chemical structure of the claimed genus but dictated by other events i.e. that pancreatic adenocarcinoma or HCC is developed in a host. For example, Kondoh et al., (01 October 1999, Cancer Research, vol. 59, pages 4990-4996) teach eight cDNAs. They encode galectin 4 (Gal-4), UGT2B4 (UDP-glucuronosyltransferase), ribosomal phosphoprotein P0 (rpP0), dek, insulin-like growth factor binding protein (IGFBP) 1, vitronectin, retinoic acid-induced gene E (RIG-E), and CYP3A4 (cytochrome P450 nifedipine oxidase), all differentially expressed genes in human hepatocellular carcinoma (HCC) as compared to the normal control of matched nontumorous liver tissues. Examination of the each of the eight cDNAs identified by Kondoh et al., indicates that none of the sequences of alectin 4 (Gal-4), UGT2B4 (UDP-glucuronosyltransferase), ribosomal phosphoprotein P0 (rpP0), dek, insulin-like growth factor binding protein (IGFBP) 1, vitronectin, retinoic acid-induced gene E (RIG-E), and CYP3A4 (cytochrome P450 nifedipine oxidase) has at least about 60 % to the instant SEQ ID NO: 1 or 3, and would hybridizes to SEQ ID NO: 1 or 3 under the recited condtions in the instant claim 1, although all of the isolated nucleic acids of Kondoh et al., have the identical function (i.e., a corresponding mRNA is differentially expressed in human hepatocellular carcinoma) recited in the instant claim: This clearly demonstrates that there is no correlation between the claimed structure and the recited function.

Qiu et al., (2003, American Journal of Pathology, vol. 162, pages 1961-1974) also teach that one of skill in the study of gene expression in HCC would not know the necessary core structure of instant SEQ ID NO: 1 or 3 in order to have the recited function. Qiu et al., on page 1965 discloses 59 human genes whose corresponding mRNAs are differentially expressed in human HCC.

Examination of the 59 different nucleic acids disclosed at Table 1 of Qiu et al., reveals that there are no structural similarities to each other, but all expressed in human HCC. All have different biological functions. None of the 59 different nucleic acids that meet the functional characteristics recited in the claimed genus in instant claim 1 meets the structural limitation. All are totally unrelated structures from each other. Thus, the instantly recited functional characteristic would not give any clues as to the claimed structure. For example, one of the nucleic acids in Table 1 of Qiu et al., has the biological function of encoding a dehydrogenase, which mobilizes hydrogen atom, the other encodes a zinc-finger binding protein. The function of GADD45 beta (an isoform of GADD45 gene) differentially expressed in human HCC is to encode a protein whose biological function is to control cellular proliferation. Qiu et al., clearly demonstrate a differential expression in human HCC is not the function of the nucleic acids disclosed in Table 1.

Further, applicant's own peer-reviewed journal publication, Choong et al., FEBS Lett. 2001 May 11;496(2-3):109-116 describing how applicant came to possess the nucleic acid as shown in Fig 2, which comprises the instant SEQ ID NO: 2, that instant SEQ ID NO: 1 encodes a protein whose function is to control transcription or translation.



Thus, differential expression in HCC is not the function associated with instant SEQ ID NO: 1 or 3.

In summary, there is no correlation between the structure of the genus of the claimed nucleic acids and the differential expression in human HCC. Which genes are being expressed in a human HCC have to be determined experimentally as disclosed at pages 1962-1965 of Qiu et al., or pages of 109- 111 of Choong et al. Thus, the instantly claimed partial structure in the form of the percent similarities along with the recited hybridization conditions, and the functional characteristics recited in claim 1 have no correlations.

As stated above, a review of the full content of the specification indicates the specification does not disclose a representative number of species” or “disclosure or relevant identifying characteristics, such as structure or other physical and/or chemical properties”, and/or describing functional characteristics coupled with a known or disclosed correlation between function and structure. The functional characteristic recited is uncoupled with the structure of the claimed genus. There is no correlation between the chemical structure of the claimed genus and the recited function.

Therefore the recited functional language describing the claimed genera does not adequately describe the common feature of claimed generic nucleic acid molecule. In addition, the specification does not give any guidance as to which domains or residues of SEQ ID NO: 1 or 3 are critical for the recited expression. In other words, the specification fails to provide any guidance as to which 595 nucleotides (60 % of 894

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nucleotides in SEQ ID NO: 1) is required for expression in a human HCC or pancreatic carcinoma.

Although the specification discloses a method for the construction of nucleic acid molecules comprising a non-naturally occurring nucleotide sequence for protein expression purposes, and making such non-naturally occurring nucleotide using recombinant DNA technology is well known in the art, the high skill in the recombinant DNA technology is not applicable to predict which structure is correlated to the recited function. Consider this situation: one of skill in the art would easily change the third nucleotide of codon #2, i.e. GCG to GCA, GCC, or GCT to make a DNA construct encoding the same protein encoded by the instant SEQ ID NO: 1 or 3. However, this high skill of one in the recombinant DNA technology is not applicable as stated previously during the prosecution history, because the instant claim as currently construed excludes the hypothetical new recombinant nucleic acid sequence encoding the instant SEQ ID NO: 2 with the second codon of, for example, GCA, instead of GCG as in SEQ ID NO: 1, if the nucleic acid is determined not to be expressed in HCC or pancreatic adenocarcinoma. One of skill has no way of knowing whether an allelic variant in the human gene encoding the instant SEQ ID NO: 2 exists, i.e. some patient has GCA, GCC, or GCT instead of GCG. There appears to be no assay available to determine whether the instant SEQ ID NO: 2 with the second codon of GCA exists naturally or being expressed differentially. Determination of existence of such a naturally occurring allelic variant at the specific position (i.e. the third position of the second codon of the gene encoding instant SEQ ID NO: 2) requires population study,

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followed by experimental validation of the specific allelic variant expression. Note page 1857-61 of Shuen et al., 2003, Genome Research, vol. 13, pages 1855-1862.

The court has dealt with similar issue in deciding *University of California v. Eli Lilly*, 43 USPQ2d 1398. The court stated that the specification from University of California failed the written description requirement of the patent law, because the University of California specification only provides the protein sequence of human insulin, and rat cDNA encoding the rat insulin, not the human cDNA itself. The court clearly stated that the specification fails to provide an adequate written description for the naturally occurring nucleic acid species (i.e. a human cDNA encoding a human insulin), even in the case that the entire protein sequence that should be encoded by the corresponding cDNA was disclosed in the specification. The court stated providing a method of obtaining the cDNA by means of a constructive example, although might be providing an enabling disclosure, nevertheless does not provide an adequate written description. The court in deciding another DNA case in *Fiers v. Revel* (CAFA) 25 USPQ 2d 1601 stated that "a mere wish or plan for obtaining the claimed invention" does not satisfy written description requirement.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1 and 3, does not reasonably provide enablement for any other nucleic acid molecules having at least 60% identity to and also hybridizes to full SEQ ID NO:1 or 3 under conditions of 0.1 x SSC buffer, 0.1% w/v SDS, at a temperature of at least 65 °C. The specification does not enable any person

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skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is A undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a genus of nucleic acid molecule with certain degree of similarity to SEQ ID NO: 1 or 3 that must be expressed differentially in HCC or pancreatic adenocarcinoma. The relative level of skill in the art in predicting a structure of DNA being differently expressed in human HCC, given a structure of a sequence is not high as demonstrated by Qui et al (cited above), and Kondoh et al (cited above). Both Qui et al., and Kondoh et al., demonstrate there is no structural simulation in order to be differently expressed in human HCC s. In other words, how to arrive at DNA structure whose corresponding structure is differentially and preferentially expressed in HCC or pancreatic carcinoma is not high; this still requires screening a large quantity of clinical samples as demonstrated by applicant's own peer reviewed journal article cited above. In order to make the claimed genus, one skilled in art has to determine what other mRNA species are differentially or preferentially expressed in HCC or pancreatic adenocarcinoma. As stated above in the written description

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rejection, which other similar sequences are differentially expressed in HCC or pancreatic adenocarcinoma is still unpredictable until said sequences are experimentally determined by screening a large quantity of appropriate clinical samples, since recombinant DNA technology is useless in making the claimed genus, because anything naturally expressed is excluded from the claimed invention. The breadth of the claim is broad including unknown species of isoforms, allelic variants, paralogs, and their fragments. The amount of direction or guidance by the inventor how to make the full scope of claimed nucleic acid molecule with the recited structural element coupled with the recited function is limited. The specification does not provide any guidance to which 60 % amino acids are necessary for the recited function. There are no working examples or guidance or direction to allow the person of ordinary skill in the art to make species in a manner commensurate in scope with the claims. The quantity of experimentation needed to make the invention is large as demonstrated by the current state of art in isolating cDNA being differentially expressed in HCC. Note the written description rejection above. In order to make the full scope of the invention, one skilled in the art has to screen a large quantity of clinical samples from liver or pancreatic tissue of patients having HCC or pancreatic adenocarcinoma, followed by sequence the nucleic acid composition.

Considering the broad scope of the claim, and the limited teachings of the specification as to which similar structure whose corresponding mRNA would be differentially expressed in HCC, it is concluded that undue experimentation would be required to enable the full scope of the claims.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. 102(e) being anticipated by US 6,639,063 B1 (Edwards et al), with the effective filing date of 05 August 1999 to US Provisional 60/147,499.

Claim 1 is drawn to an isolated nucleic acid comprising a nucleotide sequence having at least about 60% similarity to the full length of SEQ ID No: 3 and that hybridizes to the complement of SEQ ID NO: 1, or 3 under the conditions of 0.1 x SSC buffer, 0.1 % w/v SDS at 65 degree Celsius, wherein an mRNA corresponding to said nucleic acid is differentially expressed in human HCC.

The '063 patent teaches an isolated nucleic acid comprising a nucleotide sequence having at least about 60% similarity to the full length of SEQ ID No: 3 and that hybridizes to SEQ ID NO: 3 under the recited conditions. Note page 1 of Exhibit A for the sequence alignment.

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Claims 1, and 15-17 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2002/0102638 (Rosen et al), with the effective filing date of 03 January 31, 2000 to US Provisional 60/179,065, and 04 February 2000 to US Provisional 60/180,628.

The claims are drawn to SEQ ID NO: 1, 3 and nucleic acid encoding SEQ ID NO: 2, wherein the mRNA corresponding to the nucleic acid are differentially expressed in human HCC.

Rosen et al., teach an isolated nucleic acid, i.e. SEQ ID NO: 90, which is 100 % identical to the instant SEQ ID NO:1. Note attached Exhibit B. The instant specification teaches SEQ ID NO: 3 is a fragment of SEQ ID NO: 1, and also teach SEQ ID NO: 1 encodes SEQ ID NO: 2. Thus, SEQ ID NO: 80 of Rosen et al., anticipates instant claims 1, 15-17.

The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the isolated nucleic acid of the prior art does not possess the same the functional characteristics of the instantly claimed nucleic acid. Since the claimed structure and the structure of the prior art are the same, it is the Office's position that the structure of the prior art inherently possesses the recited function. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed nucleic acid is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

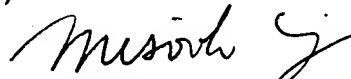
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**Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
MISOOK YU, Ph.D.  
Examiner  
Art Unit 1642



George C. Elliott, Ph.D  
Director  
Technology Center 1600



10624

Qy	67	AAAGCAAGATATGCTTCTGCTGGTTTGGAGCACAAGGGAATTAAGCAAGATCTTATCGA	126
Db	6381	AAAGCAAGATATGCTT - CTTGTGGTTTGGAGACCAAGGGAATTAAGCAAGATCTTATCGCA	6323
Qy	127	CAGACTCCAGGCATATCTTGAAGAAATGCTGAAGAGGAGGCAATTAAGAGAGATGTACT	186
Db	6322	CAGCTCCAGGCATATCTTGAAGAAATGCTGAAGAGGAGGCAAT - - - GAGATGTACT	6266
Qy	187	GGAGAGTAAACAGAGGAAGAAGAAACAAGCCCATTTGAGCTCTCTGTCTCAAGAGGAAGA	246
Db	6265	AGGAGATGAACAGAGAAGAAAAA - - - - - AACCCGTTGTCTCAATAGGGAAGA	6219
Qy	247	ACCCCTCG - AAAAAATGTTTGATGTGCGACGACAGAAGAAATGTGTGAAATATACATCTG	305
Db	6218	ACCCCTCGAAAAAATGTTTGATGTGCGACGACAGAAGAAATGTGTGAAATATACATCTG	6159
Qy	306	AAATACCACAGACTGAGAGAATCAGAGAGGCTTGAACGATTCAAATGTATCTGTGAGCT	365
Db	6158	AAATACCACAGGCTGAGAGAATCAGAGAGGCTCGAACAAATTCAGTGTATCTGTGAGCT	6099
Qy	366	TGAGAGTAAGAAGCTGCTCGGGCAGCTAGTGGTTTGGGATTTCTTCAGTTCACACAAAG	425
Db	6098	TGAGAGTAAGAAGCTGCTCAGGCGAGTATAGTTTGGGATTTCTTCAGTTCACACAAAN -	6040
Qy	426	GTCTGTATCTGATATAACAACCTATAGTTAACTTGGATTAAGCTGAAGGAAGAGCTCAAA	485
Db	6039	GTCTGTATCTG - - AACACACCTATGGTTNACTTGGATTAAGCCGAGGAAGAGCTCAAA	5982
Qy	486	GATTTGGTTTGAATGCTGTTTCAATCTCCAGAAAGTCTGAAGATGATGAAGAACTGA	545
Db	5981	GATTTGGTTTGAATGCTGTTTCAATTTCCAGAAAGTCTGAAGATGATGAAGAACTGA	5922
Qy	546	AGAGGAAGAGCGATTTGGGATTTGTCACAGTTTCAGCTGGAACTGGAAACACACAGAGATA	605
Db	5921	AGAGGAAGAGCGATTTGGGATTTGTCACAGTTTCAGCTGGAACTGGAAACACACAGAGATA	5862
Qy	606	CAGAGGCAAGAGAAGAAAAAGCAGAGCGCTTTTGGGATTTGCTCATGAAAAAGTTCCTG	665
Db	5861	CAGAGGCAAGAGAAGAAAAAGCAGAGCGCTTTTGGCATTGCTCATGAAAAAGTTCCTG	5802
Qy	666	ATATCTTCTGTTCTCCAGTGTGTTTCAATTTCTCTCTTCTTCTTGGTTCACATATATGCT	725
Db	5801	ATATCTTCTGTTCTCCAGTGTGTTTCCACTTCTCTCATTTCTTCTGGTTCACATATATACTA	5742
Qy	726	AAATGCACAGTCATGTGCCCTACGCTCTGCTCGCAATGAGGGAGCAGTGTACCCAGGTAC	785
Db	5741	AA - - - - - TGCAGTCTGTGCCCTTGCATGAGGGAGCAGGTATACCCAGGTAA	5698
Qy	786	ATCCATGAATCGGGCAGCAGATTGTGACTTATTTCTGTTCAGCTTTTAAGGTTTGTGTGTT	845
Db	5697	AATGTGTGACTCGCGGCAGTTTGGACTTATTTGCTGTTTCAGCTTTTAAGGTTTGTGTGTT	5638
Qy	846	TTTGTGTTTTGATTAATGTTGCTTGT 870	
Db	5637	TTTGTGTTTTGATTAATGTTGCTTGT 5613	

RESULT 3  
US-09-621-976-3627  
; Sequence 3627 Application US/09621976  
; Patent No. 6639063  
; GENERAL INFORMATION:  
; APPLICANT: Dumas Milne Edwards, J.B.  
; APPLICANT: Jobert, S.  
; APPLICANT: Giordano, J.Y.  
; TITLE OF INVENTION: ESTs and Encoded Human Proteins  
; FILE REFERENCE: GENSET.054PR2  
; CURRENT APPLICATION NUMBER: US/09/621,976  
; CURRENT FILING DATE: 2000-07-21  
; NUMBER OF SEQ ID NOS: 19335  
; SOFTWARE: Patent.pm  
; SEQ ID NO 3627  
; LENGTH: 553

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? APPLICANT: Giordano, J.Y.
? TITLE OF INVENTION: ESTs and Encoded Human Proteins
? FILE REFERENCE: GENSET.054PR2
? CURRENT APPLICATION NUMBER: US/09/621,976
? CURRENT FILING DATE: 2000-07-21
? NUMBER OF SEQ ID NOS: 19335
? SOFTWARE: Patent.pm
? SEQ ID NO 3627
? LENGTH: 553
?

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2 of 4

;; TYPE: DNA  
;; ORGANISM: Homo sapiens  
;; FEATURE:  
;; NAME/KEY: CDS  
;; LOCATION: 36..452  
US-09-621-976-3627

Query Match 60.1%; Score 525; DB 4; Length 553;  
Best Local Similarity 99.8%; Pred. No. 4.1e-152;  
Matches 536; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

QY 1 TGGAGTGGGGTAAACAAGATGGCGACCGAGCGGTGGAGCTCCATAGCTTAAAGCTTGC 60  
DB 17 TGGAGTGGGGTAAACAAGATGGCGACCGAGCGGTGGAGCTCCATAGCTTAAAGCTTGC 76  
QY 61 CGAAGTAAAGCAAGAAATGCTTGTCTCGTGGTGGAGACCAAGGCAATAAAGCAAGATCT 120  
DB 77 CGAAGTAAAGCAAGAAATGCTTGTCTCGTGGTGGAGACCAAGGCAATAAAGCAAGATCT 136  
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QY 241 GGAAG 300  
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DB 317 ATCTGAATATCCACAGACTGAGAGATGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 376  
QY 361 GAGCTTGGAGAGTAAAG 419  
DB 377 GAGCTTGGAGAGTAAAG 436  
QY 420 CAAAGAGTCTGTCATCTGATTAACAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 479  
DB 437 CAAAGAGTCTGTCATCTGATTAACAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 496  
QY 480 CTCAAGAGATTTGGTTGAATGCTCTTCAATCTCCAGAGAGAGAGAGAGAGAGAGAGAG 536  
DB 497 CTCAAGAGATTTGGTTGAATGCTCTTCAATCTCCAGAGAGAGAGAGAGAGAGAGAGAG 553

RESULT 4

US-09-513-999C-736  
; Sequence 736, Application US/09513999C  
; Patent No. 6783961  
; GENERAL INFORMATION:  
; APPLICANT: Dumas Milne Edwards, J.B.  
; APPLICANT: Duciart, A.  
; APPLICANT: Giordano, J.Y.  
; TITLE OF INVENTION: Expressed Sequence Tags and Encoded Human Proteins.  
; Patent No. 6783961  
; FILE REFERENCE: 59 US2 REG  
; CURRENT APPLICATION NUMBER: US/09/513,999C  
; CURRENT FILING DATE: 2000-02-24  
; PRIOR APPLICATION NUMBER: US 60/122,487  
; PRIOR FILING DATE: 1999-02-26  
; NUMBER OF SEQ ID NOS: 36681  
; SOFTWARE: Patent.pm  
; SEQ ID NO 736  
; LENGTH: 471  
; TYPE: DNA  
; ORGANISM: Homo sapiens  
; FEATURE:  
; NAME/KEY: CDS  
; LOCATION: 25..471  
; FEATURE:

;; NAME/KEY: misc\_feature  
;; LOCATION: 354  
;; OTHER INFORMATION: y=c or t  
US-09-513-999C-736

Query Match 53.3%; Score 465.6; DB 4; Length 471;  
Best Local Similarity 99.8%; Pred. No. 9.2e-134;  
Matches 465; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 TGGAGTGGGGTAAACAAGATGGCGACCGAGCGGTGGAGCTCCATAGCTTAAAGCTTGC 60  
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QY 61 CGAAGTAAAGCAAGAAATGCTTGTCTCGTGGTGGAGACCAAGGCAATAAAGCAAGATCT 120  
DB 66 CGAAGTAAAGCAAGAAATGCTTGTCTCGTGGTGGAGACCAAGGCAATAAAGCAAGATCT 125  
QY 121 TATCCACAGACTCCAGGCAATATCTTGAAGACATCTGGAAGAGGAGGCAATGAAGAAGA 180  
DB 126 TATCCACAGACTCCAGGCAATATCTTGAAGACATCTGGAAGAGGAGGCAATGAAGAAGA 185  
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DB 186 TGTAAGTGGAGATGAAACAGAGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 245  
QY 241 GGAAG 300  
DB 246 GGAAG 305  
QY 301 ATCTGAATATCCACAGACTGAGAGATGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 360  
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QY 361 GAGCTTGGAGAGTAAAG 420  
DB 366 GAGCTTGGAGAGTAAAG 425  
QY 421 AAAAGGTCTGTCATCTGATTAACAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 466  
DB 426 AAAAGGTCTGTCATCTGATTAACAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 471

RESULT 5

US-09-621-976-18639  
; Sequence 18639, Application US/09621976  
; Patent No. 6639063  
; GENERAL INFORMATION:  
; APPLICANT: Dumas Milne Edwards, J.B.  
; APPLICANT: Jobert, S.  
; APPLICANT: Giordano, J.Y.  
; TITLE OF INVENTION: ESTs and Encoded Human Proteins.  
; FILE REFERENCE: GENSET.054PR2  
; CURRENT APPLICATION NUMBER: US/09/621,976  
; CURRENT FILING DATE: 2000-07-21  
; NUMBER OF SEQ ID NOS: 19335  
; SOFTWARE: Patent.pm  
; SEQ ID NO 18639  
; LENGTH: 405  
; TYPE: DNA  
; ORGANISM: Homo sapiens  
; FEATURE:  
; NAME/KEY: misc\_feature  
; LOCATION: 126..127  
; OTHER INFORMATION: n=a, g, c or t  
US-09-621-976-18639

Query Match

Best Local Similarity 42.9%; Score 374.2; DB 4; Length 405;  
Matches 383; Conservative 11; Mismatches 7; Indels 2; Gaps 1;

QY 2 GGAGTGGGGTAAACAAGATGGCGACCGAGCGGTGGAGCTCCATAGCTTAAAGCTTGC 61  
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665000-000000  
filed 02/26/1999

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Gln Ala Tyr Leu Glu Glu His Ala Glu Glu Glu Ala Asn Glu Glu Asp
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cct gtc aaa gag gaa gaa ccc cct gaa aaa act gtt gat gtg gca gca 293
Pro Val Lys Glu Glu Glu Pro Pro Glu Lys Thr Val Asp Val Ala Ala
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3 17 21

; CURRENT APPLICATION NUMBER: US/09/621,976  
 ; CURRENT FILING DATE: 2000-07-21  
 ; NUMBER OF SEQ ID NOS: 19335  
 ; SOFTWARE: Patent.pm  
 ; SEQ ID NO 7487  
 ; LENGTH: 139  
 ; TYPE: PRT  
 ; ORGANISM: Homo sapiens  
 US-09-621-976-7487

Query Match 60.1%; Score 625; DB 4; Length 139;  
 Best Local Similarity 100.0%; Pred. No. 4.2e-51;  
 Matches 126; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
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 DB 1 MATETVELHLKLAELKQECCLARGLETGKIGKQDLIHLQAYLEHAEHEEEDVLGDET 60  
 QY 61 EBEETKPIELPVKEEPEPKTDVAAEKVKVKTSEIPQTERMQKRAERFNVPSLESKK 120  
 DB 61 EBEETKPIELPVKEEPEPKTDVAAEKVKVKTSEIPQTERMQKRAERFNVPSLESKK 120  
 QY 121 ARAAR 126  
 DB 121 ARAAR 126

## RESULT 3

US-09-270-767-42868  
 ; Sequence 42868, Application US/09270767  
 ; Patent No. 6703491  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Homburger et al.  
 ; TITLE OF INVENTION: Nucleic acids and proteins of Drosophila melanogaster  
 ; FILE REFERENCE: File Reference: 7326-094  
 ; CURRENT APPLICATION NUMBER: US/09/270,767  
 ; CURRENT FILING DATE: 1999-03-17  
 ; NUMBER OF SEQ ID NOS: 62517  
 ; SOFTWARE: PatentIn Ver. 2.0  
 ; SEQ ID NO 42868  
 ; LENGTH: 343  
 ; TYPE: PRT  
 ; ORGANISM: Drosophila melanogaster  
 ; FEATURE:  
 ; OTHER INFORMATION: xaa means any amino acid  
 US-09-270-767-42868

Query Match 13.8%; Score 143.5; DB 4; Length 343;  
 Best Local Similarity 24.4%; Pred. No. 1.7e-05;  
 Matches 61; Conservative 39; Mismatches 81; Indels 69; Gaps 10;  
 QY 7 ELHLKLAELKQECCLARGLETGKIGKQDLIHLQAEHEEHEEHEEED 54  
 DB 18 DVTQKQVADLKRRLKGLAVNGKTELQDLQALLEGDSLSDSAIADDDVSFT 77  
 QY 55 -----VLGDETEEEETK-PIELPVKEEPEPKTDVAAEKVKVKTSEIPQTERMQK- 106  
 DB 78 DEDEHLKLGNDDELKPKSPVSTTTVAIP-----DLAEK-----TSSAPDAAPTCKI 128  
 QY 107 -----AERFNVPSLESKKAARAFGLISSVPTKGLSSDNKPMV----- 145  
 DB 129 VLKRNNSQOSTGVASTGTPP-SKENEPAAASDSTGETPTK-----KHKPIVVGPKTEG 183  
 QY 146 -----NLDKLKERAFGLNVSSISKSDDSKLKRERFGIVTSSAGTGT 192  
 DB 184 EKPSGDKLNQTAQRIELRAKFGITPPAVA-NTATAVAIVANKSSASITANKNGE 242  
 QY 193 TETDEAKRK 202  
 DB 243 TEEQKEASK 252

## RESULT 4

US-09-538-092-1242  
 ; Sequence 1242, Application US/09538092  
 ; Patent No. 6753314  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Giot, Loic  
 ; TITLE OF INVENTION: Protein-Protein Complexes and Method of Using Same  
 ; FILE REFERENCE: 15966-542  
 ; CURRENT APPLICATION NUMBER: US/09/538,092  
 ; CURRENT FILING DATE: 2000-03-29  
 ; PRIOR FILING DATE: 1999-04-01  
 ; PRIOR APPLICATION NUMBER: 60/127,352  
 ; PRIOR FILING DATE: 2000-02-01  
 ; NUMBER OF SEQ ID NOS: 1387  
 ; SOFTWARE: CurapatSeqFormatter Version 0.9  
 ; SEQ ID NO 1242  
 ; LENGTH: 824  
 ; TYPE: PRT  
 ; ORGANISM: Homo sapiens  
 ; FEATURE:  
 ; NAME/KEY: misc feature  
 ; LOCATION: (0)-(0)  
 ; OTHER INFORMATION: Polypeptide Accession Number Q00839  
 US-09-538-092-1242

US-09-538-092-241  
 ; Sequence 241, Application US/09538092  
 ; Patent No. 6753314  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Mansfield, Traci A.  
 ; TITLE OF INVENTION: Protein-Protein Complexes and Method of Using Same  
 ; FILE REFERENCE: 15966-542  
 ; CURRENT APPLICATION NUMBER: US/09/538,092  
 ; CURRENT FILING DATE: 2000-03-29  
 ; PRIOR FILING DATE: 1999-04-01  
 ; PRIOR APPLICATION NUMBER: 60/127,352  
 ; PRIOR FILING DATE: 1999-04-01  
 ; PRIOR APPLICATION NUMBER: 60/178,965  
 ; PRIOR FILING DATE: 2000-02-01  
 ; NUMBER OF SEQ ID NOS: 1387  
 ; SOFTWARE: CurapatSeqFormatter Version 0.9  
 ; SEQ ID NO 241  
 ; LENGTH: 218  
 ; TYPE: PRT  
 ; ORGANISM: Saccharomyces cerevisiae  
 ; FEATURE:  
 ; NAME/KEY: misc feature  
 ; LOCATION: (0)-(0)  
 ; OTHER INFORMATION: Polypeptide Accession Number YER063W  
 US-09-538-092-241

Query Match 12.1%; Score 125.5; DB 4; Length 218;  
 Best Local Similarity 22.0%; Pred. No. 0.0044;  
 Matches 52; Conservative 38; Mismatches 81; Indels 65; Gaps 8;  
 QY 11 LKLAELKQECCLARGLETGKIGKQDLIHLRL-----QAYLEHAEHEEHEEED 54  
 DB 7 LTVVLQDLKLLTKRNLSVGLKKNELVQLIKDDEESKGESEVSPQSQNQEQSGSEPAIEEP 66  
 QY 55 VLGDETEEEETKPIELPVKEEPEPKTDV-----AAEKVKVKTSEIPQTERMQ 104  
 DB 67 ASQNIETKKEVS--SEPKETNEPKENKDVQKPSDGPSTASENEQAAATAAPALSPEE 124  
 QY 105 KRAERFNVPSLESKKAARAFGLISSVPTKGLSSDNKPMVNLDKLKERAFGLNVSS- 163  
 DB 125 IKAK-----ALDLNKLKLRANKFG-----QDQADISLQRIINRVEKFGVDLNSK 170  
 QY 164 -----ISRKSEDE-----KLKRXERFGIVTSSAGTGTTEDEAKRKRAERFG 208  
 DB 171 LAELGLVSRKNEPESGNGKFKNRK-----NANRNRVSVKRGNRSG 215

RESULT 5  
 US-09-538-092-1242  
 ; Sequence 1242, Application US/09538092  
 ; Patent No. 6753314  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Giot, Loic  
 ; TITLE OF INVENTION: Protein-Protein Complexes and Method of Using Same  
 ; FILE REFERENCE: 15966-542  
 ; CURRENT APPLICATION NUMBER: US/09/538,092  
 ; CURRENT FILING DATE: 2000-03-29  
 ; PRIOR FILING DATE: 1999-04-01  
 ; PRIOR APPLICATION NUMBER: 60/127,352  
 ; PRIOR FILING DATE: 2000-02-01  
 ; NUMBER OF SEQ ID NOS: 1387  
 ; SOFTWARE: CurapatSeqFormatter Version 0.9  
 ; SEQ ID NO 1242  
 ; LENGTH: 824  
 ; TYPE: PRT  
 ; ORGANISM: Homo sapiens  
 ; FEATURE:  
 ; NAME/KEY: misc feature  
 ; LOCATION: (0)-(0)  
 ; OTHER INFORMATION: Polypeptide Accession Number Q00839  
 US-09-538-092-1242

Exhibit B

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RESULT 2  
US-09-764-846-90  
; Sequence 90, Application US/09764846  
; Patent No. US20020102638A1  
; GENERAL INFORMATION:  
; APPLICANT: Rosen et al.  
; TITLE OF INVENTION: Nucleic Acids, Proteins, and Antibodies  
; FILE REFERENCE: PZ12  
; CURRENT APPLICATION NUMBER: US/09/764, 846  
; CURRENT FILING DATE: 2001-01-17  
; Prior application data removed - consult PALM or file wrapper  
; NUMBER OF SEQ ID NOS: 348  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 90  
; LENGTH: 1154  
; TYPE: DNA  
; ORGANISM: Homo sapiens  
; FEATURE:  
; NAME/KEY: SITE  
; LOCATION: (1149)

OTHER INFORMATION: n equals a.t.g, or c  
US-09-764-846-90  
Query Match 100.0%; Score 894; DB 9; Length 1154;  
Best Local Similarity 100.0%; Pred. No. 2.1e-229;  
Matches 894; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
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QY 61 CTTGCCGAATCAAAGCAAGAAATCTCTGCTGCTGGTGGAGACCAAGGGAATAAAGCAA 120  
DB 237 CTTGCCGAATCAAAGCAAGAAATCTCTGCTGCTGGTGGAGACCAAGGGAATAAAGCAA 296  
QY 121 GATCTTATCCACAGATCTCCAGGAGATCTTGAAGAGAGAGAGAGAGAGAGAGAGAG 180  
DB 297 GATCTTATCCACAGATCTCCAGGAGATCTTGAAGAGAGAGAGAGAGAGAGAGAGAG 356  
QY 181 GAAGATGTACTGGGAGATGAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 240  
DB 357 GAAGATGTACTGGGAGATGAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 416  
QY 241 AAAG 300  
DB 417 AAAG 476  
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DB 477 ATTACATCTGAATATCCACAGATCTGAAGAGAGAGAGAGAGAGAGAGAGAGAGAG 536  
QY 361 CTTGTGAGCTTGGAGAGTGAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 420  
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QY 481 AGAGCTCAAGAGATTTGGTTGAATGCTCTTCAATCTCCAGAGAGAGAGAGAGAGAG 540  
DB 657 AGAGCTCAAGAGATTTGGTTGAATGCTCTTCAATCTCCAGAGAGAGAGAGAGAGAG 716  
QY 541 AAACCTGAAAG 600  
DB 717 AAACCTGAAAG 776  
QY 601 ACAGAGGATACAG 660  
DB 777 ACAGAGGATACAG 836  
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RESULT 3  
US-10-091-483-90  
; Sequence 90, Application US/10091483  
; Publication No. US20030049650A1  
; GENERAL INFORMATION: